

EXHIBIT 1, Tab 6b

5.2.2 HYDROTHERAPY

Hydrotherapy is one of the oldest forms of treatment for patients with arthritis. Despite this, formal evidence showing benefit is sparse. Limited evidence suggests that hydrotherapy can effect and maintain an improvement in self-efficacy in addition to some clinical and psychological gain.^{172, 173} A recent systematic review of balneotherapy¹⁷⁴ (i.e. hydrotherapy or spa therapy) noted that no conclusion could be provided from the reviewed studies due to poor methodology. Further well-conducted trials are needed to assess the efficacy of this mode of treatment.

5.2.3 OTHER PHYSICAL THERAPIES

Evidence for other therapies such as the application of ice or heat,¹⁷⁵ TENS or laser therapy¹⁷⁶⁻¹⁷⁹ is conflicting or is insufficient to support their routine use. There is limited evidence showing symptomatic benefit from ultrasound.¹⁸⁰

5.3 SPLINTING

Splinting can be undertaken by occupational therapists, physiotherapists, or orthotists. Good evidence to support the use of resting hand splinting is sparse although two studies did report a significant reduction in pain when splints were applied.^{181,182} Wrist working splints have been shown to decrease pain on activity^{183,184} but do not improve function, grip strength or dexterity.^{185,186} There is no good evidence to support the use of splints to correct ulnar deviation or any other deformity.

Evidence level 1⁺



Resting and working splints can be used to provide pain relief.

5.4 PODIATRY

The importance of appropriate footwear provision for comfort, mobility and stability is well recognised in clinical practice but there is little evidence-based research to support such observations in patients with early RA.

There is some evidence regarding the efficacy of foot orthoses in terms of both comfort level and stride speed and length.¹⁸⁷⁻¹⁸⁹

The guideline development group could find no research regarding other podiatry interventions such as reduction of callosities and padding of the feet in those with early RA.

- ☒ Podiatry referral should be offered to all patients.

5.5 DIETETICS

Nutritional advice plays an important part in the management of a patient with RA. Enquiries about diet are amongst those most commonly received from patients.

5.5.1 WEIGHT MANAGEMENT

Weight reduction in obese individuals is important particularly when weight bearing joints are involved. Management should be as recommended in the SIGN guideline on obesity.¹⁹⁰

Cachexia may occur in those with severe active RA. The aetiology is likely to be multifactorial. Several studies have shown that patients with low body mass index (BMI) do less well and have poorer functional status.^{191,192} Whilst it is not clear whether dietary intervention improves outcome, for general health reasons, an adequate BMI should be maintained. Some patients will require diet supplements in addition to dietary advice.

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5.5.2 DIET AS THERAPY

Relatively few studies have been carried out to assess the effect of diet therapy on disease activity in RA.¹⁹³ Fasting has been shown to be of benefit in some patients.¹⁹⁴ Weight loss often occurs and this may not be beneficial in all patients. Practical difficulties have also been encountered in implementing and maintaining strict dietary changes. The evidence regarding food exclusion is often anecdotal and is inconclusive. Exclusion/elimination diets can be difficult to follow and if adhered to over a long period of time, may lead to the development of nutritional deficiencies.

5.5.3 DIET SUPPLEMENTS

A meta-analysis of clinical trials of fish oil supplementation in RA concluded that there was a significant reduction in the number of tender joints and in duration of morning stiffness after three months of therapy. However, no effect was seen on indices of disease activity or progression of RA.¹⁹⁵ There are practical limitations to this approach, including the large quantities of fish oil required. The latter is expensive, difficult to take and not available on prescription.

The effect of other oils such as evening primrose oil¹⁹⁶ and blackcurrant seed oil¹⁹⁷ on disease activity in RA remains uncertain.

Annex 1

DETAILS OF SYSTEMATIC REVIEW UNDERTAKEN FOR THE GUIDELINE

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by the SIGN Information Officer in collaboration with members of the guideline development group.

Searches were restricted to systematic reviews, meta-analyses, randomised controlled trials, and longitudinal studies. Inclusion criteria were patients with rheumatoid arthritis within five years of diagnosis, aged over 16. Exclusion criteria were studies based outside Western Europe, Scandinavia, North America, Australia or New Zealand; surgery; psychological treatments; social care or social support of patients.

Searches were carried out on the Cochrane Library, Embase, Medline, and Pascal from 1985 onwards. A subsearch on alternative or traditional therapies also looked at the Allied & Alternative Medicine and Mantis databases. All search strategies were evaluated by an independent information specialist.

The main searches were supplemented by material identified by individual members of the development group. All selected papers were evaluated using standard methodological checklists before conclusions were considered as evidence.

The question of late harm caused particular difficulties in searching. The section of the strategy on this topic focused on the long-term toxicity or toleration of DMARDs. It is recognised that this limited approach does not fully cover the literature on this subject, but given the restricted time available to complete the development process it was decided to accept this limitation.

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Annex 2

AMERICAN RHEUMATISM ASSOCIATION 1987 REVISED CRITERIA FOR THE CLASSIFICATION OF RHEUMATOID ARTHRITIS¹⁶

Diagnosis of rheumatoid arthritis requires four of seven of the following criteria. In criteria one to four the joint signs or symptoms must be continuous for at least six weeks.

Signs & Symptoms	
1. Morning stiffness	Duration > 1hr lasting > 6 weeks
2. Arthritis of 3 or more joint areas*	Soft tissue swelling or effusion lasting > 6 weeks
3. Arthritis of hand joints	Wrist, metacarpophalangeal joints or proximal interphalangeal joints lasting > 6weeks
4. Symmetric arthritis*	At least one area, lasting > 6 weeks
5. Rheumatoid nodules	As observed by a physician
6. Serum rheumatoid factor	As assessed by a method positive in less than 5% of control subjects
7. Radiographic changes	As seen on anteroposterior films of wrists and hands

* Possible areas: proximal interphalangeal joints, metacarpophalangeal joints, wrist, elbow, knee, ankle, metatarsophalangeal joints (observed by a physician).

At least four criteria must be fulfilled.

Annex 3

CRITERIA FOR COMPLETE REMISSION IN RA

Complete remission is achieved with five of the following six:

1. morning stiffness < 15 minutes
2. no fatigue
3. no joint pain (history)
4. no joint tenderness or pain on motion
5. no soft tissue swelling in joint/tendon sheaths
6. Westergren ESR < 30mm/hr (F) < 20mm/hr (M)

Exclusion: extra-articular disease

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Annex 4

HEALTH ASSESSMENT QUESTIONNAIRE¹⁷

Patient Label

Date

We are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comments at the end of this form.

PLEASE TICK ONE RESPONSE WHICH BEST DESCRIBES YOUR USUAL ABILITIES OVER THE PAST WEEK:

- | | Without
ANY
difficulty
<i>Score = 0</i> | With
SOME
difficulty
<i>Score = 1</i> | With
MUCH
difficulty
<i>Score = 2</i> | Unable
to do
<i>Score = 3</i> |
|---|--|--|--|-------------------------------------|
| 1. DRESSING AND GROOMING
- <i>Are you able to</i>
Dress yourself, including tying shoelaces and doing buttons?
Shampoo your hair? | | | | |
| 2. RISING - <i>Are you able to</i>
Stand up from an armless straight chair?
Get in and out of bed? | | | | |
| 3. EATING - <i>Are you able to</i>
Cut your meat?
Lift a full cup or glass to your mouth?
Open a new carton of milk (or soap powder)? | | | | |
| 4. WALKING - <i>Are you able to</i>
Walk outdoors on flat ground?
Climb up five steps? | | | | |

PLEASE TICK AIDS OR DEVICES THAT YOU USUALLY USE FOR ANY OF THESE ACTIVITIES:

Walking stick	Crutches
Devices for dressing e.g. buttonhook, zipper pull, long handled shoe horn	Special or built-up chair
Walking frame	Wheelchair
Built-up or special utensils	Other (please specify)

PLEASE TICK ANY CATEGORIES FOR WHICH YOU USUALLY NEED HELP FROM ANOTHER PERSON:

Dressing and grooming	Rising	Eating	Walking
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HEALTH ASSESSMENT QUESTIONNAIRE *continued*

Without ANY difficulty Score = 0	With SOME difficulty Score = 1	With MUCH difficulty Score = 2	Unable to do Score = 3
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5. HYGIENE - *Are you able to*

Wash and dry your entire body?

Take a bath?

Get on and off the toilet?

6. REACH - *Are you able to*Reach and get down a 5lb object
(e.g. a bag of potatoes) from
above your head?Bend down to pick up clothing
from the floor?**7. GRIP - *Are you able to***

Open car doors?

Open jars which have been
previously opened?

Turn taps on and off?

8. ACTIVITIES - *Are you able to*

Run errands and shop?

Get in and out of a car?

Do chores such as vacuuming,
housework or light gardening?**PLEASE TICK AIDS OR DEVICES THAT YOU USUALLY USE FOR ANY OF THESE ACTIVITIES:**

Raised toilet seat	Jar opener (for jars previously opened)	Long handled appliances for reach
Bath seat	Bath rail	Other (please specify)

PLEASE TICK ANY CATEGORIES FOR WHICH YOU USUALLY NEED HELP FROM ANOTHER PERSON:

Hygiene	Reach	Gripping and opening things	Errands and housework
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SCORING OF HAQ

Add the maximum score for each of the 8 sections and divide by 8 to give a score between 0–3.
If aid/device or help is needed the score for that activity automatically = 2 (unless 3 has already
been ticked.)

Normal function = 0

Most affected function = 3

Annex 5

EVALUATION OF DMARD EFFECT

1. ACR IMPROVEMENT CRITERIA¹⁹⁸

- tender joint count*
- swollen joint count*
- at least three of:
 - global disease activity – investigator
 - global disease activity – patient**
 - patient assessment of pain
 - physical disability score, e.g. HAQ
 - acute phase reactant

ACR 20, ACR 50 and ACR 70 indicate 20%, 50% and 70% improvement in the above

* extent of synovitis is measured by doing a count of number of tender joints and number which are both swollen and tender.

** patient opinion of disease activity measured on a 10 cm visual analogue scale. Anchor points at either end of the scale are 'not active at all' and 'extremely active'.

2. EULAR RESPONSE CRITERIA¹⁹⁹

Disease activity score (DAS) is derived using a nomogram which incorporates the following four measures:

- Ritchie articular index²⁰⁰
- swollen joint count
- ESR (Westergren)
- general health score

DAS > 2.8 is usual level of activity for enrolment in DMARD studies

Interpretation of change in disease activity score from baseline evaluation of response:

- > 1.2 good
- > 0.6 moderate ≤ 1.2
- ≤ 0.6 non-responder

3. RADIOLOGICAL ASSESSMENT

Sharp method²⁰¹ (scores erosions and joint space narrowing)

Larsen method²⁰² (utilises standardised films that illustrate progressive destructive disease)

Annex 6

Awareness of and vigilance for drug interactions is important, but concern about drug interactions should not prevent the prescription of drugs that are needed to reduce joint damage in early RA. Much more morbidity will accrue from leaving RA untreated than will occur as a result of these interactions.

DRUG INTERACTIONS WITH NSAIDs

Drug	Effect of NSAID on drug	Principal mechanism*
Antihypertensives (ACE Inhibitors, Angiotensin II receptor antagonists)	Therapeutic effect decreased Hyperkalaemia and renal impairment increased	Sodium retention Interference with intrarenal prostaglandins
Warfarin	Therapeutic effect increased	Displaced protein binding Inhibition of drug metabolism
Sulphonylureas	Therapeutic effect increased	Displaced protein binding
Cyclosporin	Risk of nephrotoxicity increased	
Methotrexate	Therapeutic effect increased	Reduced renal clearance
Digoxin	Therapeutic effect increased	Reduced renal clearance
Lithium	Therapeutic effect increased	Reduced renal clearance
Phenytoin	Therapeutic effect increased	Displaced protein binding

Risk of GI haemorrhage is increased in patients on warfarin or corticosteroids. Further interactions are listed in the British National Formulary, Appendix 1⁵⁸

** the mechanisms underlying drug interactions are complex*

DRUG INTERACTIONS WITH DMARDs

Drug	Interacts with
Azathioprine	Allopurinol Co-trimoxazole, trimethoprim, rifampicin Possibly warfarin
Hydroxychloroquine	Amiodarone Antiepileptics Digoxin
Cyclosporin	Multiple drugs, grapefruit juice
D-penicillamine	Antacids, zinc, iron (including proprietary indigestion tablets or mixtures) <i>N.B. should not be taken together</i>
Sulphasalazine	Digoxin
Methotrexate	Aspirin/NSAIDs Co-trimoxazole, trimethoprim, phenytoin All antifolate drugs Cyclosporin
Leflunomide	Phenytoin Warfarin Tolbutamide Other hepatotoxic/haemotoxic drugs
Minocycline	Antacids, zinc, iron Cyclosporin

Further interactions are listed in the British National Formulary, Appendix 1⁵⁸

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Annex 7

EXTENT OF RESPONSE TO SINGLE AGENTS IN RECENT DMARD STUDIES

Drug	Dose	no. in study	median disease duration	median duration of study	proportion achieving response	
					ACR 20 [†]	ACR 50 [†]
Sulphasalazine ¹³⁰	2-3 g/day	68	1 year	1 year	59%	[34%]*
Sulphasalazine ⁸⁵	2 g/day	133	7 years	0.5 year	44%	30%
Methotrexate ¹³⁰	7.5-15 mg/day	69	1.5 years	1 year	59%	[38%]*
Methotrexate ⁹⁶	7.5-15 mg/day	182	6 years	1 year	35%	23%
Methotrexate ¹³⁹	7.5-20 mg/day	217	1 year	1 year	65%	42%
Leflunomide ⁸⁵	20 mg/day	133	8 years	0.5 year	48%	33%
Leflunomide ⁹⁶	20 mg/day	182	7 years	1 year	41%	34%
Etanercept ¹³⁹	10 mg twice weekly (subcutaneous)	208	1 year	1 year	64%	32%
Etanercept ¹³⁹	25 mg twice weekly (subcutaneous)	207	1 year	1 year	72%	48%

*figures in [] reflect Dougados report of EULAR "good" responders

[†] see Annex 5

Annex 8

RECOMMENDATIONS FOR FURTHER RESEARCH

The following are suggested as potential areas for further research:

GENERAL

1. The definition of early RA.
2. Clarification of the important factors for diagnosis and prognosis.
3. Inception cohort studies to investigate the combination of prognostic factors that will predict disease severity in individual patients and allow patients suitable for early aggressive therapy to be identified.
4. Evaluation of new imaging techniques to assess early joint damage.
5. Audit of referral time from symptom onset to rheumatology clinic appointment: resource implications of delay before specialist review.

PHARMACOLOGICAL MANAGEMENT

NSAIDs

1. Further evaluation of highly selective Cox2 agents:
 - will they reduce the incidence of ulcer complications in routine clinical practice?
 - will it be necessary for GI protective agents to be co-prescribed in patients at high risk of ulcer complications?
 - what effect will they have on NSAID- associated renal and cardiovascular events?
2. NSAIDs which block nitric oxide synthetase.

DMARDs

1. The optimum treatment strategy for achieving remission in early RA using existing/new DMARDs. This should include:
 - the most appropriate action if a patient fails to achieve an adequate response to methotrexate or sulphasalazine
 - long term, adequately powered studies of the combination of methotrexate and sulphasalazine in early disease
 - prospective study of other combination options
 - assessment of long term safety issues.

CORTICOSTEROIDS

1. Long term, adequately powered studies to investigate whether continuous low-dose prednisolone and step-down prednisolone regimens will reduce joint damage/disability in the long term.
2. Assessment of cumulative toxicity.

TNF BLOCKADE AND NOVEL THERAPIES

1. The role of anti-TNF therapy in the treatment of patients with early RA:
 - as 'bridge therapy' to induce remission while waiting for DMARDs to take effect
 - in combination with DMARD therapy when there has been insufficient beneficial effect
 - as monotherapy in RA
 - the optimal dosage and method of administration of anti-TNF therapy and the issue of immunogenicity

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- efficacy of anti-TNF agents in preventing joint damage and maintaining function over the longer term
 - long term data on whether anti-TNF therapy will increase susceptibility to infection or tumours
 - pharmacoeconomic analyses of anti-TNF therapy including indirect costs associated with RA (e.g. disability and unemployment).
2. Evaluation of future possibilities for biological therapy in RA, such as:
 - IL-1 receptor blockade with recombinant human IL-1 receptor antagonist
 - blockade of IL-6 receptors
 - anti-inflammatory cytokines such as IL-10 and IL-4
 - targeting T-cells e.g. anti-CD4 antibodies.
 3. Evaluation of matrix metalloproteinase inhibitors in early RA.

THE ROLE OF THE MULTIDISCIPLINARY TEAM

1. Evaluating early intervention by the multidisciplinary team versus medical care alone and the impact on functional ability.
2. Evaluation of rheumatology nurse specialist role.
3. Physiotherapy
 - compliance with exercise and its relationship to longer term outcome
 - the effect of exercise training programmes on muscle strength and function
 - inpatient versus outpatient physiotherapy in the management of early RA.
4. Occupational therapy
 - efficacy of joint protection techniques.
5. Splinting
 - short and longer term evaluation of resting and working splints.
6. Podiatry
 - effect of foot orthoses on foot deformity and pain.
7. Dietetics
 - RCTs of dietary supplements such as antioxidants
 - further research on the possible drug-sparing effect of fish oils.
8. Pharmacy
 - the role of the pharmacist in patient education about drug therapy
 - the pharmacist's role in monitoring for drug interaction and side effects.

PATIENT INVOLVEMENT

1. The emotional impact of being diagnosed with RA and the value of psychological input.
2. Assessment of patient attitudes to early aggressive treatment.
3. Strategies to try to maintain patient employment: vocational assessment and retraining if necessary.
4. RCTs of educational interventions including patient led self-management courses in early RA (evaluating their impact on disability and emotional distress).
5. RCTs of psychological therapy such as cognitive behavioural therapy in early RA (evaluating their impact on disability and emotional distress).

OTHER ASPECTS

1. RCTs of complementary therapies in early RA evaluating benefit and harm.
2. Homeopathy in early RA.

Annex 9

KEY MESSAGES FOR PATIENTS

These key messages are not intended for direct dissemination to patients, but are provided for possible use by clinicians in discussing treatment options with patients who have RA. They may be incorporated into local patient information materials, an example of which is shown in Annex 10.

- In RA joints become inflamed making them painful, swollen and stiff.
- The cause of RA is unknown.
- There is no single test to diagnose RA.
- RA cannot be cured at present, but in many cases it can be controlled.
- The progression of RA is different in each person.
- RA can be treated; reducing pain, stiffness, swelling and damage to joints.
- The sooner RA is treated the better, the earlier treatment is started the less damage takes place in the joints, meaning less restriction on carrying out normal activities.
- Treatment with DMARDs should begin as soon as possible after diagnosis.
- DMARDs take several weeks to start working and should be continued indefinitely.
- The treatment of RA requires input from a range of health professionals.

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Annex 10

EXAMPLE PATIENT INFORMATION LEAFLET

WHAT IS RHEUMATOID ARTHRITIS (RA)?

RA is a disease that makes your joints become painful, swollen and stiff. This is caused by inflammation taking place in the joints. Inflammation is normally caused by our body's immune system when we are injured or have an infection. We do not know what causes the immune system to cause inflammation in the joints.

HOW IS RA DIAGNOSED?

There is no single test for diagnosing RA. The diagnosis is made from the information you give the doctor as well as the information gained from examining you and the results of blood tests and x-rays.

CAN RA BE CURED?

RA cannot be cured at present, but for many patients it can be controlled.

HOW WILL RA AFFECT ME IN THE FUTURE?

At present it is not possible to predict for an individual person how their RA will affect them in the future. Some people have very mild RA which causes few problems. Others have some pain and stiffness in their joints and occasional flare-ups when their joints become more painful and swollen. This can lead to damage to the joints. Some people will have to modify their activities in some way. A small number of people develop significant problems.

CAN RA BE TREATED?

Yes.

Treatment for RA can:

- help with the pain, stiffness and swelling in joints
- reduce damage to joints
- help people stay able to do all the things they want to.

HOW CAN RA BE TREATED?

Treating RA is a partnership between you, your GP and your rheumatologist. Treatment does not just involve taking tablets. A team of health professionals is also important. These include: nurse specialist, physiotherapist, occupational therapist, pharmacist, dietitian, podiatrist (chiropodist) and social worker.

You can help by knowing as much as you can about RA and its treatment. If you know about your tests, drugs and the need to watch for side effects, your outlook will be better.

WHEN SHOULD I START TREATMENT FOR RA?

The sooner the better.

The earlier treatment is started the less damage takes place in the joints and the more likely that you will be able to continue your usual activities.

WHAT MEDICATION SHOULD I HAVE?

- **Painkillers** such as paracetamol, cocodamol and coproxamol may help with pain. It is important that you do not take more than the maximum recommended dose. Painkillers other than paracetamol may cause constipation.
- **Nonsteroidal anti-inflammatory drugs (NSAIDs)** such as ibuprofen, diclofenac, naproxen, indomethacin, nabumetone, etodolac, meloxicam, rofecoxib and celecoxib, help with the pain, swelling and stiffness in your joints, but do not stop damage occurring to your joints. There are many different NSAIDs and not all NSAIDs suit everyone. You may have to try several different drugs before you find one that helps you. The main side effect of NSAIDs is indigestion. Sometimes inflammation or ulceration of the stomach or intestine can occur. This may very rarely cause bleeding. If you experience indigestion or have previously had a stomach ulcer you should discuss this with your doctor. Sometimes additional treatment to protect the gastrointestinal tract is needed.
- **Disease modifying anti-rheumatic drugs (DMARDs)** include sulphasalazine, methotrexate, gold, penicillamine, hydroxychloroquine, azathioprine, cyclosporin and leflunomide. You should start on a DMARD as soon as possible after being diagnosed with RA. DMARDs are not painkillers, but over time they should help with the pain and stiffness in your joints and make you feel better. DMARDs are very important because they slow down damage to your joints and reduce disability. DMARDs take some weeks to start working. It is important to continue taking them, even if they do not seem to be working at first. You will be fully informed about the potential risks and benefits of DMARDs. You will be given written information about any DMARD that your doctor has suggested you start. Most DMARDs require regular blood tests and sometimes urine tests in order to look out for side effects. You should be given a card or monitoring sheet on which the results of your blood tests can be recorded.
- **Steroid injections** into joints can help with the pain and swelling in that joint. Rest after injection may result in additional benefit. Sometimes when you have many inflamed joints, steroid will be given as an injection into your muscle.
- **Steroid tablets**, such as prednisolone, are sometimes necessary, but they have potential side effects. They help with symptoms and may prevent joint damage in the short term, but most people who are on steroid tablets for a long time suffer from side effects. These include thinning of bones (osteoporosis), thinning of skin and putting on weight.

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HOW LONG SHOULD I CONTINUE ON TREATMENT?

Usually you should stay on treatment with a DMARD for as long as the drug continues to work, provided that you do not develop side effects which are serious or troubling. If this happens then an alternative DMARD will be recommended by your rheumatologist.

Most patients need to keep taking a DMARD in order to stop their arthritis from flaring up and to slow down damage occurring to the joints. Hopefully, if your joint pain improves on the DMARD then you will be able to take fewer painkillers and perhaps stop your NSAID.

SHOULD I EXERCISE OR NOT?

Exercise is important. It can reduce joint pain and stiffness and keep your muscles strong. This will improve your level of fitness and make you feel better. All patients with RA should see a **physiotherapist** for advice about suitable exercises which may be carried out on dry land or in water (hydrotherapy).

SHOULD I CONTINUE TO WORK?

It is important not to make decisions about work too soon. Modern therapy should allow control of your disease and continuation of employment even if hours and activities require modification.

WHAT OTHER TREATMENTS SHOULD I HAVE?

- **Occupational therapists** can advise you about different ways of carrying out many everyday activities. This helps to protect your joints. In addition you can be given simple aids to help with certain tasks.
- Wrist splints can help with pain.
- Footwear is important. Shoes that are comfortable and support your feet are helpful. You can be referred to a **podiatrist** (chiroprapist) and/or orthotist to be supplied with cushioned insoles or better fitting shoes.
- It is helpful if you can be your ideal bodyweight. This is based on your height and your doctor or nurse specialist can advise you about this. A **dietitian** can give you advice about losing weight if you are overweight or putting weight on if you are too thin.

IS THERE A DIET THAT WILL HELP RA?

At present there is no evidence from scientific studies to support changing to any particular diet.

DO ANY HERBAL OR COMPLEMENTARY MEDICINES HELP RA?

Supplements of fish oil may help the symptoms of RA, but do not stop joint damage. Large quantities of fish oil are required. Other complementary medicines have not been shown to be of benefit in RA. Many complementary medicines have not been tested in good quality scientific studies. Complementary medicines may have side effects.

Annex 11

USEFUL ORGANISATIONS/SUPPORT GROUPS

ARTHRITIS RELATED ADDRESSES AND WEBSITES

Arthritis Canada	www.arthritis.ca
Arthritis Care Phoenix House, 7 South Avenue, Clydebank Business Park, Clydebank, G81 2LG Tel: 0141 952 5433 Fax: 0141 952 5433	www.arthritiscare.org.uk
American College of Rheumatology	www.rheumatology.org
Arthritis Foundation of Ireland 1 Clanwilliam Square, Grand Canal Quay, Dublin 2, Ireland Tel: (+353) 01 6618188 Fax: (+353) 01 6618261	www.arthritis-foundation.com
Arthritis Foundation (USA)	www.arthritis.org
Arthritis Research Campaign (ARC) Copeman House, St Mary's Court, St Mary's Gate, Chesterfield, Derbyshire S41 7TD Tel: 01246 558033 Fax: 01246 558007	www.arc.org.uk
British Health Professionals in Rheumatology c/o BSR, 41 Eagle St, London WC1R 4AR Tel: 0171 242 3313 Fax: 0171 242 3277	www.rheumatology.org.uk/BHPR
British Society of Rheumatology 41 Eagle Street, London WC1R 4AR Tel: 020 7 242 3313 Fax: 020 7 242 3277 (includes the British Society for Rheumatology, British Institute of Musculoskeletal Medicine, British Orthopaedic Association, Society for Back Pain Research, the Arthritis and Rheumatism Council for Research)	www.rheumatology.org.uk
European League Against Rheumatism (EULAR) EULAR Secretariat, Witikonstrasse 15, CH-8032 Zürich, Switzerland Tel: +41 1 383 96 90 Fax: +41 1 383 98 10	www.eular.org
The British League against Rheumatism (BLAR) c/o The British Society for Rheumatology (see above)	
International League of Associations for Rheumatology (ILAR)	www.ilar.org
University of Birmingham, Dept of Rheumatology	www.rheuma.bham.ac.uk

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OTHER USEFUL ADDRESSES AND WEBSITES

Disabled Living Foundation

380-384 Harrow Rd, London W9 2HU

www.dlf.org.uk

Health information distributed by GPs

www.healthinfofocus.co.uk

Health Education Board for Scotland

Woodburn House, Canaan Lane, Edinburgh EH10 4SG

Tel: 0131 536 5500

Fax: 0131 536 5501

www.hebs.scot.nhs.uk

Help for Help Trust (UK)

Highcroft, Romsey Road, Winchester, Hampshire SO22 5DH

Tel: 01962 849100

Fax : 01962 849079

www.hfht.org

provides consumer information and links to health sites

Medical Research Council

MRC Head Office, 20 Park Crescent, London W1N 4AL

Tel: 020 7636 5422

Fax: 020 7436 6179

www.mrc.ac.uk

National Electronic Library for Health

www.nelh.nhs.uk

Organising Medical Networked Information (OMNI)

OMNI / BIOME, Greenfield Medical Library,

Queens Medical Centre, Nottingham NG7 2UH

www.omni.ac.uk

NHS Direct

www.nhsdirect.nhs.uk

UK Health Centre

guide to health/medical information on the internet

www.healthcentre.org.uk/hc/clinic/websites/default.htm

UK reference site for the lay person

www.patient.co.uk

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Update to printed guideline

11 Oct 2004

Withdrawal of Rofecoxib

The NSAID Rofecoxib is mentioned in Section 4.2.4 and Annex 10 of this guideline. This drug has been voluntarily withdrawn from the market by the manufacturers due to concerns about a possible increased risk of heart attack or stroke. Patients currently being prescribed Rofecoxib should be transferred to a suitable alternative NSAID. Further information about the reasons for withdrawal of the drug can be found on the US Federal Drug Administration Web site at <http://www.fda.gov/medwatch/SAFETY/2004/safety04.htm#vioxx>



Management of early rheumatoid arthritis

SIGN Publication
Number **48**

Quick Reference Guide

CLINICAL FEATURES OF EARLY RHEUMATOID ARTHRITIS (RA)

Symptoms

- Joint pain/swelling
- Stiffness following inactivity
- Systemic 'flu-like' features

Signs

- Synovitis
- Joint swelling/tenderness
- Extra-articular features

INFLAMMATORY POLYARTHRITIS

Differential diagnosis

- Viral arthritis
- Reactive arthritis
- Seronegative spondyloarthropathy
- Connective tissue disease
- Polymyalgia rheumatica
- Polyarticular gout
- Fibromyalgia
- Medical conditions presenting with arthropathy

Helpful investigations

- Erythrocyte sedimentation rate (ESR) /C-reactive protein (CRP)
- Full blood count
- Urea & electrolytes
- Liver function tests
- Uric acid/synovial fluid analysis
- Urinalysis
- Rheumatoid factor
- Anti-nuclear antibody
- Radiology

Adverse prognostic features in early RA

- Many active joints
- High ESR or CRP at outset
- Positive rheumatoid factor
- Early radiological erosions
- Poorer scores of function at outset
- Adverse socio-economic circumstances and lower educational level

EARLY INITIATION OF TREATMENT

B RA should be treated as early as possible with disease modifying anti-rheumatic drugs (DMARDs) to control symptoms and delay disease progression.

- ☒ All patients with persistent inflammatory joint disease (>6-8 weeks duration) already receiving simple analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs) should be considered for referral for specialist rheumatology opinion and DMARD therapy, preferably within 12 weeks.

THE ROLE OF THE MULTIDISCIPLINARY TEAM

- ☒ All patients with early RA should have access to a range of health professionals, including general practitioner, rheumatologist, nurse specialist, physiotherapist, occupational therapist, dietitian, podiatrist, pharmacist and social worker.

C Skilled occupational therapy advice should be available to those experiencing limitations in function.

C Resting and working splints can be used to provide pain relief.

B Patients should be encouraged to undertake simple dynamic exercises.

- ☒ Podiatry referral should be offered to all patients.

KEY



indicates grade of recommendation

☒ good practice point

PHARMACOLOGICAL MANAGEMENT OF EARLY RA**NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)**

B The lowest NSAID dose compatible with symptom relief should be prescribed. NSAIDs should be reduced and if possible withdrawn when a good response to DMARDs is achieved.

B Introduce gastro-protection in RA patients >65 years and in those with a past history of peptic ulcer.

- ☒ Simple analgesics should be used in place of NSAIDs if possible and DMARDs should be introduced early to suppress disease activity.
- ☐ Only one NSAID should be prescribed at a time.
- ☐ Prescribers should be aware of the many potential interactions with NSAIDs and the side effect profiles of different drugs.
- ☐ Consider intra-articular corticosteroids, particularly when disease is localised.
- ☐ NSAIDs should be avoided in patients taking anticoagulants or corticosteroids.

DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDs)

B Early DMARD therapy in RA is important to maintain function and reduce later disability.

B DMARD therapy should be sustained in inflammatory disease in order to maintain disease suppression.

- ☒ DMARD choice should take into account patient preference and existing co-morbidity.

B Sulphasalazine, methotrexate, IM gold, and penicillamine are equally effective DMARDs.

B Sulphasalazine and methotrexate are the current DMARDs of choice due to their more favourable efficacy/toxicity profiles.

B At present the balance of evidence does not support the routine use of combination DMARD therapy in early RA.

- ☒ Patients should be counselled about the benefits and risks of specific DMARDs, and should be provided with additional written information.
- ☒ Clear advice about monitoring of specific DMARDs should be available to the patient, GP and practice nurse.

CORTICOSTEROID THERAPY

B Oral corticosteroids are not recommended for routine use, as there is no sustained clinical or functional benefit and there is high risk of toxicity with long term use.

D The lowest possible dose of corticosteroid should be used for the shortest possible time.

D Monitor patients closely for adverse corticosteroid effects. Be alert to the possibility of diabetes, cataract and infection. Inform patients not previously infected of the danger of chicken pox/shingles exposure.

- ☒ Inform patients of the risks of corticosteroids prior to prescription and issue a steroid warning card.

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